PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| PWO-19174 | | |
| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
| PCT/JP00/00018 | 06/01/2000 | 07/01/1999 |
| International Patent Classification (IPC) or national classification and IPC<br>C07D335/02 | | |
| Applicant<br>FUJISAWA PHARMACEUTICAL CO., LTD. et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 21/07/2000 | 30.03.2001 |
| Name and mailing address of the international preliminary examining authority:<br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized officer<br>Grassi, D<br>Telephone No. +49 89 2399 8499 |

Form PCT/IPEA/409 (cover sheet) (January 1994)

13.4.-3

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP00/00018

## I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
**Description, pages:**

1-294 as originally filed

**Claims, No.:**

1-17 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 13,14,16,17 (with respect to industrial applicability).

because:

☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 6-17 |
| | No: | Claims | 1-5 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-17 |
| Industrial applicability (IA) | Yes: | Claims | 1-12,15 |

No: Claims

2. Citations and explanations
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
**see separate sheet**

**Re Item III**

Claims 13, 14, 16 and 17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**Re Item V**

1) Reference is made to the following documents:
D1: I. STAHL ET AL.: '2,2-DISUBSTITUIERTE 1,3-DITHIANE' CHEMISCHE BERICHTE., vol. 113, no. 2, 1980, pages 800-5, XP002151298 VERLAG CHEMIE GMBH. WEINHEIM., DE ISSN: 0009-2940
D2: US-A-5 747 514 (a copy is attached)

2) The subject-matter of present claims 1-5 is not new (Article 33(2) PCT).
The compounds **3e, f** and **11c, d** of D1 fall within the terms of the said claims.

3) The novel part of claims 1-4 and the claims 6-9 do not involve an inventive step (Article 33(3) PCT).

D2 discloses compounds inhibiting metalloproteinases and the release of tumor necrosis factor (cf. abstract).
The problem underlying the present application is seen in the provision of alternative compounds exhibiting said properties.

The present description shows that one compound (example 15) exhibits the alleged activity.
Having regard to the very broad terms of the present claims it is not credible that essentially all of the claimed compounds solve the technical problem (A contains 2 to 6 carbon atoms, $R^1$ encompasses any heterocyclic group with no limitation to ring size or substituents, Ar encompasses any aromatic group with no limitation to ring size or substituents, $R^1$ encompasses any carboxy or amid residue).

The applicant is therefore requested to submit further test data supporting the

breath of the present claims or to restrict the claims to a group of compounds for which the alleged activity is credible.

4) The claims 10-17 would only be regarded as involving inventive activity if the claim 1 fulfilled said requirement.

5) For the time being, the **novel part** of claim 5 is regarded as inventive. In view of the active compound of example 15, it is credible that the group of compounds according to claim 5 exhibits similar properties and therefore solve the technical problem.

6) For the assessment of the present claims 11-17 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Item VIII**

1) The invention appears not to be sufficiently disclosed (Art. 5 PCT). Compounds according to the present claims 1-5 in which X is oxa, $R^1$ is halogen and Y/Z are thia appear not to be stable. The description does not enable the skilled person prepare such compounds.

2) The present claims are not clear (Art. 6 PCT).

2.1) The term "lower" is not clear.

2.2) The term "lower alkenyl" in connection with fragment A is not clear.

2.3) The claim 7 contains an error. It appears that $R^1$ (cf. page 309, line 31) should be replaced by $R^{11}$.